JOINT DEGENERATION: MOUSE MODELS

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PARTICIPATING ORGANIZATION:
National Institutes of Health (NIH)
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COMPONENTS OF PARTICIPATING ORGANIZATION:
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
(http://www.niams.nih.gov/)
National Institute on Aging (NIA)
(http://www.nia.nih.gov/)
National Institute of Dental and Craniofacial Research (NIDCR)
(http://www.nidcr.nih.gov/)

CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBERS: 93.846, 93.866, 93.121

THIS PA CONTAINS THE FOLLOWING INFORMATION

PURPOSE OF THIS PA

This announcement solicits proposals of research employing genetically defined and genetically modified mouse models to explore the biological mechanisms underlying non-inflammatory joint degeneration, or osteoarthritis. Inflammatory processes are evident in late stages of osteoarthritis, and are likely to be major contributors to the chronic pain that is the most common symptom of the condition. However, for the

purpose of this initiative, osteoarthritis is distinguished from diseases, such as rheumatoid arthritis, in which inflammation arising from autoimmunity is the primary cause of tissue damage. In contrast, the root causes of joint degeneration in osteoarthritis remain unclear. Increasing knowledge of molecular mechanisms in cartilage and bone biology, along with advances in the genetic manipulation of mice, have yielded new concepts and new animal models that may be relevant to osteoarthritis in humans. This Program Announcement is intended to accelerate the characterization of new models and the testing of hypotheses that could lead to improved diagnosis and treatment of osteoarthritis.

RESEARCH OBJECTIVES

Background

Osteoarthritis is the most common form of arthritis and the major cause of activity limitation and physical disability in older people. Current treatments for osteoarthritis are largely palliative, and many cases eventually require replacement of the joint with a prosthesis. Joint replacement is costly, and the finite functional life of prostheses can make a second replacement necessary, compounding the cost and risk for associated morbidity. Efforts to develop methods for the surgical or biological repair of damaged articular cartilage face major obstacles, owing to the limited intrinsic repair capacity of the tissue. Thus, much could be gained if the root causes of joint degeneration could be identified. Risk assessment or diagnosis at early stages of disease progression, coupled with the development of preventive or therapeutic interventions, could reduce health care costs and substantially improve the quality of life for older people. The development of preventive strategies and early-stage interventions for osteoarthritis is likely to depend upon the identification of the molecular and cellular mechanisms that underlie progressive deterioration of joint structure and function.

Osteoarthritis is characterized by degeneration of the articular cartilage surfaces of a joint. Within the cartilage environment, this degeneration is reflected in the functional decline and apoptosis of chondrocytes, and by elevated levels of proteases known to participate in the breakdown of extracellular matrix. The development of osteoarthritis is strongly correlated with age. Yet there is evidence that joint degeneration is not an inevitable consequence of aging, and that the factors influencing joint structure and function are complex. The knee and hip are more often affected than other joints, and one hip or knee may be more seriously affected than the other in the same individual. Genetic factors may predispose some individuals to develop osteoarthritis. The mechanical history of a joint, including both normal patterns of use and traumatic injury, is likely to be a major factor.

Recent observations suggest that it may be helpful to consider the joint as an integrated structure of bone and cartilage. During skeletal development, the hypertrophic chondrocytes of growth plates normally undergo apoptosis, and cartilage is degraded and replaced by bone. In the regions that will become the articular surfaces of joints, cartilage is retained over a supporting region of subchondral bone. One current hypothesis is that

osteoarthritis reflects the inappropriate recurrence of the hypertrophic pathway in articular chondrocytes. The formation of bony outgrowths, or osteophytes, in osteoarthritic joints is consistent with this idea. If this hypothesis is sound, it follows that osteoarthritis may arise in part from disruption of mechanisms that establish and maintain the boundary between articular cartilage and subchondral bone. Thus, at least some of the causes of osteoarthritis may lie within the complex network of mechanisms that regulate the development and growth of the skeleton early in life.

The development of powerful methods for the genetic manipulation of mice has led to the creation of modified strains in which the consequences of specific genetic characteristics can be assessed in the intact animal and across the lifespan. In some instances, it has been reported that specific gene inactivation or over-expression results in age-related joint degeneration, with histological similarities to osteoarthritis. Several inbred mouse strains have also been observed to develop osteoarthritis-like joint degeneration with age. Because both genetic and environmental factors may be precisely defined in the laboratory, these mouse models hold the potential to reveal the genetic factors and hence the molecular pathways that influence the degeneration of joints.

Scope

This program will support research with the potential to reveal the biological mechanisms underlying non-inflammatory joint degeneration in mouse models. Research supported by this initiative will identify specific genes, proteins, and biochemical pathways that contribute to joint degeneration. Information to be gained will include the timing and anatomical location of events that lead to joint degeneration, the functional characterization of proteins identified as causal factors, and the definition of pathways by which particular gene products contribute to joint degeneration. Objectives include: the characterization of new models; the development and testing of hypotheses that arise from the properties of new and existing models; and the definition of functional roles for specific molecular entities identified as contributing to joint degeneration.

The NIDCR is interested in supporting meritorious research targeting new animal models of osteoarthritis that have relevance to the temporomandibular joint (TMJ). Applications describing animal models that elucidate molecular mechanisms of TMJ degeneration and aid in the diagnosis and treatment of TMJ Disorders are particularly encouraged. Applications addressing unique features of the TMJ including the presence of fibrocartilage on its articulating surfaces and the distinctive anatomy and mechanical loading of this joint also are of interest to the NIDCR.

Suggested research topics may include, but are not limited to:

o Molecular characterization of phenotypes of mice exhibiting joint degeneration, for example, by correlating gene expression profiles with time of onset, rate of progression, and severity;

o Identification of downstream effectors in pathways mediating effects of gene inactivation or transgene expression in genetically modified mice exhibiting joint degeneration;

o Mapping of genetic loci linked to joint degeneration in inbred mouse strains;

o Characterization of changes at the chondro-osseous junction that precede or accompany degradation of the articular surface in mouse models; or

o Testing of models of joint degeneration by specific antagonism of biological functions, using anti-sense, dominant-negative, or RNAi approaches.

MECHANISMS OF SUPPORT

This PA will use the NIH R01 and Exploratory/Developmental Research Grant (R21) award mechanisms (http://grants.nih.gov/grants/guide/pa-files/PA-03-107.html). As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. Applications using the R21 mechanism may request a project period of up to two years with a combined budget for direct costs of up $275,000 for the two year period, excluding the facilities and administrative (F&A) costs requested by consortium participants. For example, the applicant may request $100,000 in the first year and $175,000 in the second year. The request should be tailored to the needs of the project. Normally, no more than $200,000 may be requested in any single year.

This PA uses just-in-time concepts. It also uses the modular budgeting as well as the non-modular budgeting formats (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, if you are submitting an application with direct costs in each year of $250,000 or less, use the modular budget format. Otherwise follow the instructions for non-modular budget research grant applications. This program does not require cost sharing as defined in the current NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part2.htm.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

o For-profit or non-profit organizations
o Public or private institutions, such as universities, colleges, hospitals, and laboratories
o Units of State and local governments
o Eligible agencies of the Federal government
o Domestic or foreign institutions/organizations
o Faith-based or community-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into two areas: scientific/research; and financial or grants management issues.

o Direct your questions about scientific/research issues to:

William J. Sharrock, Ph.D.
Musculoskeletal Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH, DHHS
One Democracy Plaza
6701 Democracy Blvd., Suite 800
Bethesda, MD 20892-4872
Telephone: (301) 594-5055
FAX: (301) 480-4543
Email: ws19h@nih.gov

Jill L. Carrington
Musculoskeletal Biology Program
Biology of Aging Program
National Institute on Aging
NIH, DHHS
7201 Wisconsin Avenue, Suite 2C231
Bethesda, MD 20892-9205
Telephone: (301) 496-6402
FAX: (301) 402-0010
Email: carringtonj@nia.nih.gov

John W. Kusiak, Ph.D.
Director
Molecular and Cellular Neurobiology Program
Division of Basic and Translational Sciences
National Institute of Dental and Craniofacial Research
Natcher, Building 45, Room 4AN-18A
Bethesda, MD 20892-6402

Telephone: 301-594-7984
FAX: 301-480-8319
Email: kusiakj@mail.nih.gov

o Direct your questions about financial or grants management matters to:

Michael G. Morse
Deputy Chief, Grants Management Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH/DHHS
One Democracy Plaza
6701 Democracy Blvd., Suite 800
Bethesda, MD 20892-4872
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7201 Wisconsin Avenue, Suite 2N212
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Mary Daley
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Division of Extramural Activities
National Institute of Dental and Craniofacial Research
Natcher, Building 45, Room 4AN-44B
Bethesda, MD 20892-6402
Telephone: 301-594-4808
FAX: 301-480-3562
Email: daleym@mail.nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a Dun and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dunandbradstreet.com/. The D&B number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at http://grants.nih.gov/grants/dates.htm. Application deadlines are also indicated in the PHS 398 application kit.

SPECIFIC INSTRUCTIONS FOR MODULAR BUDGET GRANT APPLICATIONS: Applications requesting up to $250,000 per year in direct costs must be submitted in a modular budget grant format. The modular budget grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

SPECIFIC INSTRUCTIONS FOR APPLICATIONS REQUESTING $500,000 OR MORE PER YEAR: Applications requesting $500,000 or more in direct costs for any year must include a cover letter identifying the NIH staff member within one of the NIH institutes or centers who has agreed to accept assignment of the application.

The NIAMS imposes specific requirements on the submission of applications requesting $500,000 or more per year, superseding the NIH-wide requirements described below. The NIAMS requirements are described in detail at http://grants.nih.gov/grants/guide/notice-files/NOT-AR-03-004.html and at http://www.niams.nih.gov/rtac/grantapps/guidelines.htm. Briefly, applications are considered only for the June 1/July 1 (Cycle II) and October 1/November 1 (Cycle III) receipt dates. A potential applicant must seek NIAMS acceptance of such an application no later than March 1, for a June 1/July 1 submission, and no later than July 1, for an October 1/November 1 submission.

Applicants requesting more than $500,000 per year from other institutes or centers (ICs) must carry out the following steps:

1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as you are developing plans for the study;

2) Obtain agreement from the IC staff that the IC will accept your application for consideration for award; and,

3) Identify, in a cover letter sent with the application, the staff member and IC who agreed to accept assignment of the application.

This policy applies to all investigator-initiated new (type 1), competing continuation (type 2), competing supplement, or any amended or revised version of these grant application types. Additional information on this policy is available in the NIH Guide for Grants and Contracts, October 19, 2001 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be mailed on or before the receipt dates described at http://grants.nih.gov/grants/funding/submissionschedule.htm. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an unfunded version of an application already reviewed, but such application must include an Introduction addressing the previous critique.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within 8 weeks.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. Appropriate scientific review groups convened in accordance with the standard NIH peer review procedures (http://www.csr.nih.gov/refrev.htm) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score

o Receive a written critique
o Receive a second level review by an appropriate national advisory council or board

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to evaluate application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. The scientific review group will address and consider each of the following criteria in assigning the application's overall score, weighting them as appropriate for each application.

o Significance
o Approach
o Innovation
o Investigator
o Environment

The application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

SIGNIFICANCE: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

INNOVATION: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

INVESTIGATOR: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

ENVIRONMENT: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, the following

items will be considered in the determination of scientific merit and the priority score:

PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. (See criteria included in the section on Federal Citations, below). http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

INCLUSION OF WOMEN, MINORITIES AND CHILDREN IN RESEARCH: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria in the sections on Federal Citations, below).

CARE AND USE OF VERTEBRATE ANIMALS IN RESEARCH: If vertebrate animals are to be used in the project, the five items described under Section f of the PHS 398 research grant application instructions (rev. 5/2001) will be assessed.

ADDITIONAL REVIEW CONSIDERATIONS

Sharing Research Data

Applicants requesting $500,000 or more in direct costs in any year of the proposed research are expected to include a data sharing plan in their application. The reasonableness of the data sharing plan or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or priority score.

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research will be assessed.

AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

o Scientific merit of the proposed project as determined by peer review
o Availability of funds
o Relevance to program priorities

REQUIRED FEDERAL CITATIONS

ANIMAL WELFARE PROTECTION: Recipients of PHS support for activities involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf), as mandated by the Health Research Extension Act of 1985 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm), and the USDA Animal Welfare Regulations (http://www.nal.usda.gov/awic/legislat/usdaleg1.htm), as applicable.

HUMAN SUBJECTS PROTECTION: Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

SHARING RESEARCH DATA: Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible. http://grants.nih.gov/grants/policy/data_sharing Investigators should seek guidance from their institutions on issues related to institutional policies and local IRB rules, as well as local, state and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS: The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov). It is the responsibility of the applicant to provide, in the project description and elsewhere in the application as appropriate, the official NIH identifier(s)for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

STANDARDS FOR PRIVACY OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION: The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information," the "Privacy Rule," on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.healthypeople.gov/.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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Department of Health
and Human Services

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